REMARKS

In response to the Office Action, Applicants offer the following remarks.

Claims 1, 2, 4, 6, 7, 9 to 12, 18 to 25, 29, 31 and 39 were examined. Original claims 3, 5, 8, 13 to 17, 26 to 28, 30, 32 to 38 and 40 to 42 were previously cancelled.

Claims 1, 7, 9, 10, 12, 18 to 25 and 39 are currently amended.

Claim 6 is currently cancelled without prejudice or disclaimer and the subject matter of this claim has been incorporated into currently amended claim 1.

New claims 44 to 49, which are based on original claims 20 to 25, and new claim 43 which is directed to an embodiment of claim 19, are hereby presented.

The present patent application now comprises twenty-six (26) claims. It is believed no new matter has been added. The amendments do not narrow the scope of the claims, nor do Applicants believe that the amendments are necessary to distinguish the claimed invention from the cited patent.

1. Response to the Claim Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 2, 4, 6, 7, 9 to 12, 18 to 21, 29, 31 and 39 stand rejected under 35 U.S.C. § 112, second paragraph. This rejection is respectfully traversed.

Claim 6 has been cancelled rendering the rejection thereto moot. Claims 1, 9, 10, 12, 19, 20, 21 and 39 as amended are believed to comply with 35 U.S.C. § 112, second paragraph. Applicants believe that no new matter has been introduced by the amendment.

(a) Claim 1

The term "solubilizing group" stands rejected as allegedly having indefinite metes and bounds. This definition is further rejected as being open-ended, and thus that it is not clear what other groups would be considered a "solubilizing group". Applicants respectfully traverse. However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended claim 1 to replace "solubilizing group" with the definition set forth in original claim 6. Withdrawal of the rejection is respectfully requested.

(b) Definition of R_1

The definition of R_1 stands rejected because C_1-alkenyl and C_1-alkynyl allegedly each require at least 2 carbon atoms. Claim 1 has been amended in order to recite in pertinent part "R_1 is (C_1-C_{10}) alkyl unsubstituted or substituted by one to three hydroxy, ~~(C_1-C_{10})alkenyl~~ (C_2-C_{10})alkenyl unsubstituted or substituted by one to three hydroxy, ~~(C_1-C_{10}) alkynyl~~ (C_2-C_{10}) alkynyl...". Withdrawal of the rejection is respectfully requested.

(c) Claim 9

Claim 9 stands rejected because the limitation "amine containing heterocycle" is allegedly not clear. Applicants traverse. It is submitted that such limitation would be clear to a person skilled in the art. However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended claim 9 to recite "wherein the amine is a ring member of the heterocycle".

(d) Scope of "substituted" aryl for R_2

The scope of "substituted" aryl for R_2 stands rejected as allegedly being unclear. In particular, the specified "substituted" aryl for R_2 as defined in the specification (page 8) stands rejected as allegedly being open-ended and therefore indefinite. The scope is rejected as allegedly being exacerbated by the presence of additional classes of compounds included as substituents on the substituents. Applicants respectfully traverse.

Applicants disagree that the definition for the recited "substituted" aryl for R_2 is open-ended and indefinite or that its scope is exacerbated by the presence of additional classes of compounds included as substituents on the substituents.

As indicated by the Examiner, the recited "substituted" aryl for R_2 is explicitly defined, either in whole or in part, at specification pages 7 to 8. First the term "aryl" is defined at specification page 7 as "aromatic radicals having 3-14 ring atoms and at least one ring having a conjugated *pi* electron system. Preferably at least two, more preferably at least four, of the ring atoms are carbon atoms. For example aryl may be a C_5, C_6, C_7, C_8, C_9 or C_{10} ring. The term 'aryl' encompasses 'heteroaryl' compounds. The term 'heteroaryl' refers to an aromatic heterocyclic group usually with one or more heteroatoms selected from O, S and N in the ring. It is submitted that the person skilled in the art would not consider such a definition or others like it, to be indefinite, nor would the person skilled in the art find the scope of such definition impossible to determine.

Second, the specification further provides examples of "aryl" which are embodiments encompassed by the instantly claimed invention, namely "[e]xamples of aryl include without limitation phenyl, substituted phenyl, pyridyl, substituted pyridyl, pyridinyl, substituted pyridinyl, thiophenyl, substituted thiophenyl, furanyl, substituted furanyl, thiazole, oxazole or substituted or unsubstituted imidazole." It is submitted that the person skilled in the art would not consider such a definition or others like it, to be indefinite nor would the person skilled in the art find the scope of such definition impossible to determine.

Third, the specification further provides examples of "substitutents" that may be present on the above "aryl" and which are embodiments encompassed by the instantly claimed invention, namely "[s]uch substituents can include, for example, halogen, hydroxyl, carbonyl (such as carboxyl, ketones (including alkylcarbonyl and arylcarbonyl groups), and esters (including alkyloxycarbonyl and aryloxycarbonyl groups)), thiocarbonyl, acyloxy, alkoxyl, phosphoryl, phosphonate, phosphinate, amino, acylamino, amido, amidine, imino, cyano, nitro, azido, sulfhydryl, alkylthio, sulfate, sulfonate, sulfamoyl, sulfonamido, heterocyclyl, aralkyl, or an aromatic or heteroaromatic moiety". It is submitted that the person skilled in the art would not

consider such a definition or others like it, to be indefinite nor would the person skilled in the art find the scope of such definition impossible to determine.

Fourth, the person having general knowledge in the art of chemistry, and particularly having read the specification, would be able to determine the point of attachment of these substituents. Accordingly, there is nothing indefinite about the above definitions.

Fifth, Applicants submit that whether these claims encompass a large, albeit finite, number of compounds should be irrelevant to patentability. Applicants have made a remarkable contribution to the art, which would be unduly restricted and cause prejudice to Applicants if it were to be limited to specific or preferred embodiments.

Finally, and importantly, the courts have stated that claims should protect inventors from competitors.

> [T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process ... would not serve the constitutional purpose of promoting progress in the useful arts.

(See *In re Gaffe,* 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976); and see MPEP 2164.08.)

In other words, the constitutional purpose of the patent laws is to protect those that are the first to disclose an invention from others who seek to avoid infringement. The present inventors are the first to disclose the claimed compounds. The specification discloses numerous aryl substituents at position R_2, process for making these compounds, and methods for testing the efficacy of such compounds as effective antibiotics. It is submitted that it would not require undue experimentation by the person skilled in the art to substitute and test other aryl substituents at position R_2. Applicants respectfully submit that failure to allow the broadest reasonable interpretation of the specification as recited in the present claims "would not serve the constitutional purpose of promoting progress in the useful arts." *Ibid.*

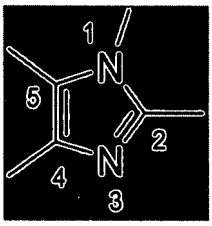
Applicants submit that the objected-to expression should not be considered open-ended, indefinite, or having exacerbated scope. Withdrawal of the rejection is respectfully requested.

(e) Claims 10, 12 and 19

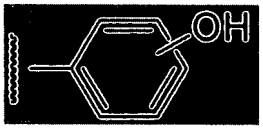
Claims 10, 12 and 19 stand rejected as allegedly reciting compounds for which their attachment to the remainder of the molecule is not known. Applicants respectfully traverse. It is submitted that the person skilled in the art would know where would be, in the recited compounds, the attachment to the remainder of the molecule.

However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended, without prejudice or disclaimer:

- claim 10 to recite in pertinent part "wherein the N-methylpiperazine is attached through its unsubstituted ring nitrogen";
- claim 12 to cancel the compounds "hydroxyethanol", "hydroxyaniline", and "4-hydroxyaniline" and to recite in pertinent part "wherein the point of attachment of 2-hydroxyethanol is at the 1 position and the point of attachment of 4-hydroxyphenyl is at the 1 position"; and
- claim 19 to recite in pertinent part "wherein R_2 is N-alkyl imidazole, wherein the point of attachment is at the 2, 4 or 5 position". It is submitted that the person skilled in the art would understand such language to be applicable as in:



Applicants submit that the person skilled in the art would understand that the point of attachment in hydroxyphenyl may be any position relative to the hydroxy substituent, as in:



where the remainder of the molecule is illustrated in the above figure by the helicoid-like structure. Withdrawal of the rejection is respectfully requested.

(f) Claims 20 and 21

Claims 20 and 21 stand rejected as allegedly being incomplete having regard to the definition of "X" in claim 1. Applicants respectfully traverse. However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended claims 20 and 21 to indicate that vinyl is *cis* or *trans*, consistent with the language of claim 1. Withdrawal of the rejection is respectfully requested.

(g) Claim 39

Claim 39 stands rejected as allegedly being unclear due to the inclusion of the word "optional". Applicants respectfully traverse. However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended claim 39 to delete the rejected word. Withdrawal of the rejection is respectfully requested.

2. Response to the Claim Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 4, 6, 7, 9 to 12, 18, 19, 29, 31 and 39 stand rejected under 35 U.S.C. § 112, first paragraph. This rejection is respectfully traversed.

The Examiner asserts that "the specification, while being enabling for making and using compounds wherein R_1 or R_2 is *phenyl*, or *hydroxyphenyl*, does not reasonably provide enablement for making and using compounds wherein R_1 or R_2 is another ring embraced in the definition of "**aryl**" or "substituted" derivatives recited for R_2 which is virtually non-limiting for many of the moieties described in specification".

Furthermore, the Examiner asserts that "[r]egarding the biological activity, the antibacterial property of the tested compounds cannot be extrapolated to other compounds

wherein R1 or R2 is other than *phenyl* as there is no evidence of recognized biological equivalency for such diverse groups" [emphasis added].

A broader claim in a patent application can be enabled by disclosure of even a single embodiment, provided that undue experimentation is not required to practice the claimed invention (see *Spectra-Physics, Inc v Coherent,* 827 F.2d 1524 (Fed. Cir. 1987) and see also; MPEP 2164.01). In addition, how a teaching is set forth, either by example or broad terminology, is not important (see MPEP 2164.08). The proscription against undue experimentation is not a proscription against some experimentation (see *Amgen, Inc. v Chugai Pharmaceutical Co., Ltd.* 927 F.2d 1200 (Fed. Cir. 1991)). Indeed, even a complex and extended period of experimentation is not undue if the art typically engages in such experimentation and/or if the specification offers guidance or sufficient direction to one of ordinary skill in the art (see MPEP 2164.01 and 2164.06).

The Examiner contends, without supporting literature, that it would require "extensive research" and a "tremendous amount of effort, time and resource" to select an effective compound from the claimed Markush group, make the compounds, determine the IC_{50} value, *in vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound.

However, Applicants submit that the claimed invention is not limited to the examples in the specification.

Many aryl groups are known in the art, and, importantly, the present specification provides a list of many such aryl groups (see specification pages 7 and 8). Thus, contrary to the Examiner's assertion, the scope of claim 1 and claims dependent thereon is not unduly broad. That other aryl substituents at position R_2 may someday be described does not mean that a claim to the aryl substituents at position R_2, as claimed and described, is unpatentable. Moreover, it is not necessary to test in working examples all of the aryl substituents at position R_2 taught in the specification (see MPEP 2164.02 and 2164.03).

Furthermore, Applicants enclose Youngman *et al.* (*J Med. Chem.* 43:346, 2000), Pagani *et al.* (*J. Med. Chem.* 43:199, 2000), Aicher *et al.* (*J. Med. Chem*, 43:236, 2000), and Almansa *et al.* (*J. Med. Chem.* 46:3463, 2003) [which are submitted herewith as part of an IDS], which were available to the skilled person in the art at the time of filing of this

application. These references are but exemplary of all the scientific literature then available to the skilled person which demonstrate retention or even enhancement of function when an aryl group is replaced with a heteroaryl group.

Pagani *et al.* teach that compounds of classes (I) and (II) containing a benzene ring and having a well-characterized antimicrobial activity (p. 199, Figure 1) are functionally equivalent (tested by MIC, *in vitro* activity against *M. avium* and *M. tuberculosis*) to compounds of classes (III-VI) in which the benzene ring is replaced with a pyridine ring (see Pagani *et al.* at page 200, left column first paragraph and Table 1).

Aicher *et al.* teach that a compound (10i) containing a phenyl group and compound (10j) in which the phenyl group is replaced with a 2-pyridyl group are functionally equivalent, *i.e.* are effective inhibitors of pyruvate dehydrogenase kinase (see Aicher *et al.* at page 241, Table 2).

Youngman *et al.* teach that a compound (8a) containing a phenyl group and compound (8b) in which the phenyl group is replaced with a 3-pyridinyl group have similar inhibitory activity as that of neuropeptide Y Y5 receptor antagonists 9 (see Youngman *et al.* at page 348, Table 1).

Almansa *et al.* teach the structures of five COX-2 inhibitors, including celecoxib (2) and etoricoxib (5) (see Almansa *et al.* at page 3463, Figure 1). The introduction of this paper states that both compounds are COX-2 selective inhibitors effective for the oral treatment of acute pain, osteoarthritis, and rheumatoid arthritis (*i.e.* they have similar functional properties notwithstanding the differences in their chemical structures).

Accordingly, and contrary to the Examiner's assertion, it was a well-known fact in the art that aryl, phenyl and heteroaryl are functional equivalents which show equivalent biological activity.

The specification discloses the procedures for formulating and testing the antibiotic compounds of the claimed invention. By following the methods both set forth in the specification and known to those of ordinary skill in the art, one of ordinary skill in the art can

easily choose additional aryl substituents at position R_2, as claimed and described, and determine whether a particular aryl substituent has antibacterial activity. The experimentation required to accomplish this is not undue and because of the teachings in the specification, there is a reasonable expectation of success. The methods are straightforward, the data analysis is unambiguous, and each test is likely to provide a quick and clear answer as to the suitability of a particular aryl substituent at position R_2.

Moreover, it is not necessary under § 112 to support every claimed embodiment with a working example (see MPEP 2164.02).

Withdrawal of the rejection is respectfully requested.

3. Response to the Claim Rejection under 35 U.S.C. § 102

Claims 1, 2, 4, 11, 29, 31 and 39 stand rejected under 35 U.S.C. § 102. This rejection is respectfully traversed with the amendment.

The Examiner asserts that these claims are anticipated by the disclosure of Hermann *et al.* (DE 2,140,280), more particularly by compound #16. Applicants respectfully traverse. However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended claims 1 and 39 to recite "with the proviso that at least one of R_3 and R_4 is halogen, and that when R_4 is halogen and R_3 is hydrogen, neither R_1 nor R_2 are alkyl".

Therefore, claims 1 and 39 are novel in view of Hermann *et al.* Because claims 2, 4, 11, 29 and 31 depend directly or indirectly on claim 1 and include all of the features of this claim, and because these claims also add additional features, which further distinguish these claims over Hermann *et al.*, claims 2, 4, 11, 29 and 31 are therefore also in condition for allowance. Withdrawal of the rejection is respectfully requested.

4. Response to Claim Objections

Claims 12, 18 and 22 to 25 stand rejected under 37 CFR 1.75(c). Applicants respectfully traverse. However, without acquiescing to the Examiner's position, and merely to advance prosecution, Applicants have amended claim 12 to delete "hydroxyaniline" and "4-hydroxyaniline", claims 22 to 25 to depend from claim 39, and claim 18 to delete "pyranyl". Withdrawal of the objections is respectfully requested.

Conclusion

Applicants submit that in view of the foregoing amendments and remarks, the claims are in condition for allowance. Such action is respectfully requested.

Respectfully submitted,

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